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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/810,333	HEEGER ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,7,8,13-16,25,28-34 and 63-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7-8, 13-16, 25, 28-34, and 63-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to the Response filed 6 May 2008 in which the specification and claim 1 was amended, claim 12 was canceled, and no new claims were added, and also in response to the Supplemental Response filed 29 July 2008 in which claims 1 and 25 amended, no claims were canceled, and new claims 63-68 were added. All of the amendments have been thoroughly reviewed and entered.

The interview summary is acknowledged and the interview record is complete.

The objections to the specification listed in the previous Office Action are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1, 7-8, 13-16, 25, 28-34, and 63-68 are under prosecution.

2. The following rejections are new rejections necessitated by the amendments.

Claim Interpretation

3. The amendments to the claims filed 6 May 2008 further limit the probe to be "an oligonucleotide probe other than an RNA nucleotide probe." Paragraph 0042 of the instant specification refers to RNA as well as "modified or synthetic" RNA. Therefore,

the limitation "an oligonucleotide probe other than an RNA nucleotide probe" in interpreted as specifically prohibiting any of an RNA probe, a "modified" RNA probe, and a "synthetic" RNA probe, and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding "an RNA probe" (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 7-8, 14-16, 25, 28-34, and 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825 B1, issued 24 July 2001) in view of Lizardi et al (U.S. Patent No. 5,312,728, issued 17 May 1994).

Regarding claim 1, Blackburn et al teach a detector. In a single exemplary embodiment, Blackburn et al teach a detector comprising an electrode capable of sensing redox events in a redox moiety in the form of a detection electrode for detecting electron transfer (column 2, lines 14-24). A probe is immobilized on the detection electrode (column 13, lines 10-13). The "capture binding ligands" of Blackburn et al are interpreted as probes because they are capture probe nucleic acids (column 40, lines 29-40), and they allow the attachment or the target analyte to the detection electrode for the purposes of detection (column 39, lines 12-65). The probes are oligonucleotides other than RNA; namely, PNA or DNA (column 8, line 65-column 9, line 30). The probe of Blackburn et al comprises a redox moiety in the form of an ETM (column 66, lines 9-44) wherein an ETM is an electron transfer moiety (i.e., redox moiety; Abstract).

Blackburn et al further teach the probe is an oligonucleotide having a hairpin stem-loop structure comprising the redox moieties 135 at an end of the probe (column 66, lines 9-44 and Figure 12), wherein either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Thus, Blackburn et al teach an embodiment wherein in the absence of the specific interaction of hybridization between the target nucleic acid with the probe, redox moiety 135 is in a first position. Upon binding to the target, the hairpin stem loop structure is altered, which moves the redox moiety to a second position. The first and second

positions give rise to distinguishable redox events detectable by the electrode because detection of the binding proceeds through the use of the ETM redox moieties (Abstract).

Blackburn et al also teach either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Therefore, one terminus of the probe is immobilized and the redox moiety 135 at the other terminus.

Blackburn et al do not teach the end of the probe bearing the redox moiety moves closer to the electrode upon binding the target; i.e., wherein the second position is closer to the electrode than the first position, thereby providing more efficient electron transfer to the electrode, or wherein the second position arises from a configuration comprising resulting from disruption of internal hybridization in the probe as a result of specific interaction between a region in the probe and the target.

However, Lizardi et al teach a single switch probe nucleic acid molecule having two alternate conformations in the presence and absence of a target molecule 8 (Figures 12-13). Lizardi et al teach the probes are molecules other than RNA probes; namely, DNA (column 6, lines 59-60). Figure 12 illustrates probe 30 in the absence of an oligonucleotide target, and Figure 13 shows the alternate conformation of the probe in the presence of the target 8. Upon binding target nucleic acid 8 (i.e., going from Figure 12 to Figure 13), specific interaction of target 8 with probe 30 disrupts internal hybridization between probe regions 32 and 33, and moves probe region 30 close to probe region 35. Figure 13 further shows internal hybridization between two regions of the probe because hairpin 36 is formed after binding to the target. Lizardi et al also

teaches the switch probes have the added advantage of allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). Thus, Lizardi et al teach the known technique wherein the configuration of a probe changes such that one end moves closer to the other end upon binding to a target as a result of disruption of internal hybridization within the probe.

While Lizardi et al do not explicitly teach that the probe of figures 12-13 is a non-RNA probe, Lizardi et al clearly teach switch probes, of which Figures 12 and 13 are one example, have the added advantage of allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). Thus, ribozyme-based detection is not specifically required of any probe. In addition, Lizardi et al clearly teach switch probes that are DNA (column 6, lines 59-65). Further, Lizardi et al clearly teach that probes of the invention of Lizardi et al contain "any desired sequence (column 15, lines 15-22)," which is interpreted to mean any probe (i.e., the DNA probes described in column 6, lines 59-65) having the sequence configuration depicted in Figures 12-13.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the detector comprising a probe having one terminus immobilized and the other terminus labeled with a redox moiety as taught by Blackburn et al with the switch probe of Lizardi et al to arrive at the instantly claimed detector with a reasonable expectation of success. The modification would

result in the probe of Lizardi et al being immobilized at end 35 as shown if Figure 12 of Lizardi et al and the redox moiety at end 32, in accordance with the end-immobilization and end-labeling taught by Blackburn et al. Upon binding, end 32 would move closer to end 35, as depicted in Figure 13, thereby promoting electron transduction to the electrode because the redox moiety is now closer to the electrode, in accordance with the embodiment described in Figure 3 and paragraph 0045 of the instant specification. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding "promoting electron transduction." The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a detector having the added advantage of having probes allowing selective generation of a detectable signal upon hybridization to the target using any number of different signal generating systems are linked to the detection of the switch as explicitly taught by Lizardi et al (Abstract and column 5, lines 15-20). In addition, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Lizardi et al could have been applied to the detector of Blackburn et al with predictable results because the probe configuration of Lizardi predictably results in probes useful for detection of target nucleic acids.

Regarding claim 7, the detector of claim 1 is discussed above. Blackburn et al further teach the probe is immobilized on the electrode on a position distant from the redox moiety because either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25) and the redox moiety 135 at the other terminus (Figure 12).

Regarding claim 8, the detector of claim 1 is discussed above. Blackburn et al further teach the electrode is capable of inducing redox events in the redox moiety; namely, the detector comprises an amperometric device for applying a potential to the electrode and different currents result because of electron transfer (column 82, lines 7-20).

Regarding claims 14-15, the detector of claim 1 is discussed above. Blackburn et al further teach the electrode comprises a metal; namely, gold (column 2, lines 60-65).

Regarding claim 16, the detector of claim 1 is discussed above. Blackburn et al further teach the redox moiety is ethidium bromide (column 49, lines 15-40).

Regarding claim 25, Blackburn et al teach a detector. In a single exemplary embodiment, Blackburn et al teach a detector comprising an electrode capable of sensing redox events in a redox moiety in the form of a detection electrode for detecting electron transfer (column 2, lines 14-24). A probe is immobilized on the detection electrode (column 13, lines 10-13). The "capture binding ligands" of Blackburn et al are interpreted as probes because they are capture probe nucleic acids (column 40, lines 29-40), and they allow the attachment or the target analyte to the detection electrode for the purposes of detection (column 39, lines 12-65). The probes are oligonucleotides other than RNA; namely, PNA or DNA (column 8, line 65-column 9, line 30). The probe of Blackburn et al comprises a redox moiety in the form of an ETM (column 66, lines 9-44) wherein an ETM is an electron transfer moiety (i.e., redox moiety; Abstract).

Blackburn et al further teach the probe is an oligonucleotide having a hairpin stem-loop structure comprising the redox moieties 135 at an end of the probe (column 66, lines 9-44 and Figure 12), wherein either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Thus, Blackburn et al teach an embodiment wherein in the absence of the specific interaction of hybridization between the target and the probe, redox moiety 135 is in a first position. Upon binding to the target, the hairpin stem loop structure is altered, which moves the redox moiety to a second position. The first and second positions give rise to distinguishable redox events detectable by the electrode because detection of the binding proceeds through the use of the ETM redox moieties (Abstract).

Blackburn et al also teach either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25). Therefore, one terminus of the probe is the instantly claimed first region that is immobilized to the electrode and the redox moiety 135 at the other terminus, which is the instantly claimed third region. The intermediate nucleotides are the second region, which form a first loop by hybridization of first and second nucleotide sequences within the second region (e.g., Figure 12).

Blackburn et al do not teach the end of the probe bearing the redox moiety moves closer to the electrode upon binding the target; i.e., wherein the second position is closer to the electrode than the first position, thereby providing more efficient electron transfer to the electrode, or wherein the second region forms a second hybridization loop upon binding the target between two regions of the probe and disrupts a first loop.

However, Lizardi et al teach a probe nucleic acid 30 that is a single molecule (Figures 12-13). Lizardi et al teach the probes are molecules other than RNA probes; namely, DNA (column 6, lines 59-60). Figure 12 illustrates the probe 30 in the absence of an oligonucleotide target, and Figure 13 shows the alternate conformation of the probe in the presence of the target. Lizardi et al teach the probe has switch sequences, which hybridize to each other in the absence of a target (column 5, lines 45-50). Figure 12 comprises element 32, wherein the terminus at 32 is the third region. Lizardi et al also teach switch sequences and probe sequences overlap (column 7, lines 47-55); thus, the second region of the instantly claimed probe comprises the remainder of element 32 as well as elements 33 and 34. The second region self hybridizes to form first loop 31 and a stem between part of 32 and 33, which are the first and second nucleotide sequences. The third region of the probe is element 35, which is located at the other end of the probe.

Upon binding target nucleic acid 8 (i.e., going from Figure 12 to Figure 13), specific interaction of target 8 with probe 30 disrupts internal hybridization between probe regions 32 and 33, and moves probe region 30 close to probe region 35. Because Lizardi et al teach switch sequences and probe sequences overlap (column 7, lines 47-55), part of 32, which is the first nucleotide sequence of the second region, also hybridizes to the target. The remaining part of 32, which is in the second region, hybridizes to part of 34, which is also part of the second region, thereby forming self-hybridized second loops 33 and 36 in the detectable structure of Figure 13. Lizardi et al also teaches the switch probes have the added advantage of allowing selective

generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). Thus, Lizardi et al teach the known technique wherein the configuration of a probe changes such that one end moves closer to the other end upon binding to a target as a result of disruption of internal hybridization within the probe.

While Lizardi et al do not explicitly teach that the probe of figures 12-13 is a non-RNA probe, Lizardi et al clearly teach switch probes, of which Figures 12 and 13 are one example, have the added advantage of allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). Thus, ribozyme-based detection is not specifically required of any probe. In addition, Lizardi et al clearly teach switch probes that are DNA (column 6, lines 59-65). Further, Lizardi et al clearly teach that probes of the invention of Lizardi et al contain "any desired sequence (column 15, lines 15-22)," which is interpreted to mean any probe (i.e., the DNA probes described in column 6, lines 59-65) having the sequence configuration depicted in Figures 12-13.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the detector comprising a probe having one terminus immobilized and the other terminus labeled with a redox moiety as taught by Blackburn et al with the switch probe of Lizardi et al to arrive at the instantly claimed detector with a reasonable expectation of success. The modification would

result in the probe of Lizardi et al being immobilized at end 35 as shown if Figure 12 of Lizardi et al and the redox moiety at end 32 in accordance with the immobilization and labeling taught by Blackburn et al. Upon binding, end 32 would move closer to end 35, as depicted in Figure 13, thereby promoting electron transduction to the electrode because the redox moiety is now closer to the electrode, in accordance with the embodiment described in Figure 3 and paragraph 0045 of the instant specification. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding "promoting electron transduction." The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a detector having the added advantage of having probes allowing selective generation of a detectable signal upon hybridization to the target using any number of different signal generating systems are linked to the detection of the switch as explicitly taught by Lizardi et al (Abstract and column 5, lines 15-20). In addition, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Lizardi et al could have been applied to the detector of Blackburn et al with predictable results because the probe configuration of Lizardi predictably results in probes useful for detection of target nucleic acids.

Regarding claim 28, the detector of claim 25 is discussed above. Blackburn et al further teach the detector comprises a detector for detecting electron transduction between the electrode and the redox moiety when the second loop is formed; namely, an AC detector (column 83, lines 55-65).

Regarding claim 29, the detector of claim 28 is discussed above. Blackburn et al also teach an indicator for inducing electron transduction; namely, an amperometric device for applying a potential to the electrode, wherein different currents result because of electron transfer (column 82, lines 7-20).

Regarding claims 30-31, the detector of claim 29 is discussed above. Blackburn et al further teach the first region is at one end of the probe and the third region is at the second end of the probe because either the 3' or 5' terminal nucleoside of the nucleic acid probe is attached to the electrode via a conductive oligomer (column 41, lines 17-25) and the redox moiety 135 at the other terminus (Figure 12)

Regarding claims 32-33, the detector of claim 25 is discussed above. Blackburn et al further teach the electrode comprises a metal; namely, gold (column 2, lines 60-65).

Regarding claim 34, the detector of claim 33 is discussed above. Blackburn et al further teach the redox moiety is ethidium bromide (column 49, lines 15-40).

Regarding claims 63-64, the detector of claim 1 is discussed above. Blackburn et al teach the probes are DNA probes (column 8, line 65-column 9, line 30) that are synthetic (Figure 9A). Lizardi et al also teach the probes are DNA (column 6, lines 59-65), and that DNA probes are chemically synthesized (column 35-40).

Regarding claim 65, the detector of claim 1 is discussed above. Blackburn et al also teach a preferred embodiment wherein the nucleic acids are PNA oligonucleotide probes (column 8, line 65-column 9, line 10).

Regarding claims 66-67, the detector of claim 25 is discussed above. Blackburn et al teach the probes are DNA probes (column 8, line 65-column 9, line 30) that are synthetic (Figure 9A). Lizardi et al also teach the probes are DNA (column 6, lines 59-65), and that DNA probes are chemically synthesized (column 35-40).

Regarding claim 68, the detector of claim 25 is discussed above. Blackburn et al also teach a preferred embodiment wherein the nucleic acids are PNA oligonucleotide probes (column 8, line 65-column 9, line 10).

7. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blackburn et al (U.S. Patent No. 6,264,825 B1, issued 24 July 2001) in view of Lizardi et al (U.S. Patent No. 5,312,728, issued 17 May 1994) as applied to claim 1 above, and further in view of Rothberg et al (U.S. Patent Application Publication No. US 2002/0012930 A1, published 31 January 2002).

Regarding claim 13, the detector of claim 1 is discussed above in Section 6.

Neither Blackburn et al nor Lizardi et al teach loops in the target and the probe in the second position (i.e., during hybridization).

However, Rothberg et al teach probes hybridized to targets wherein the probe and the target have a loop during hybridization; namely, Figure 1D, wherein the hybridized probe leaves a loop in the probe and target in the form of the gapped region and a loop in the form of the single stranded portion of the rolling circle template molecule (Figure 1D). Rothberg et al teach the loop in the target has the added advantage of allowing detection of single nucleotide polymorphisms in the gap

(paragraph 0091). Single nucleotide polymorphisms are indicative of genetic diseases. Thus, Rothberg et al teach the known technique of using a probe having loops after hybridization to a target.

It would therefore have been obvious to a person or ordinary skill in the art at the time the claimed invention was made to have modified the detector as taught by Blackburn et al in view of Lizardi et al with the loop regions in the target and the probe as taught by Rothberg et al to arrive at the instantly claimed detector with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a detector having the added advantage of allowing detection of markers of genetic disease as a result of detection of single nucleotide polymorphisms in the gap as explicitly taught by Rothberg et al (paragraph 0091). In addition, it would have been obvious to the ordinary artisan that the known technique of using the probe configuration of Rothberg et al could have been applied to the detector of Blackburn et al in view of Lizardi et al with predictable results because the probe configuration of Rothberg et al predictably results in probes useful for detection of target nucleic acids.

Response to Arguments

8. Applicant's arguments filed 6 May 2008 (hereafter the "Remarks") and the arguments filed 29 July 2008 (hereafter the "Supplemental Remarks have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on pages 12-14 of the Remarks that that the modification of the detector of Blackburn et al with the teachings of Lizardi et al would change the principle of operation of the detector of Blackburn et al and render the detector inoperable because the structure in Lizardi that is relied upon is a ribozyme, which cleaves, thereby losing the redox moiety.

However, as noted in the new rejections above (as necessitated by the amendments), Lizardi et al clearly teach switch probes, of which Figures 12 and 13 are one example, have the added advantage of allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). Thus, ribozyme-based detection is not specifically required of any probe.

In addition, Lizardi et al clearly teach switch probes that are DNA (column 6, lines 59-65).

Further, Lizardi et al clearly teach that probes of the invention of Lizardi et al contain "any desired sequence (column 15, lines 15-22)," which is interpreted to mean any probe (i.e., the DNA probes described in column 6, lines 59-65) having the sequence configuration depicted in Figures 12-13.

Therefore, Lizardi et al suggest the probes of the invention (i.e., Figures 12-13) are DNA probes and thus do not require any ribozyme activity, as the probes allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20).

Thus, contrary to Applicant's arguments on page 14 of the Remarks, the teachings of Blackburn et al and Lizardi et al have been considered as a whole.

B. Applicant's remaining arguments in pages 14-15 of the Remarks rely on the alleged deficiencies of Blackburn et al in view of Lizardi et al. These alleged deficiencies are discussed above. Since the arguments regarding the alleged deficiencies of Blackburn et al in view of Lizardi et al were not persuasive for the reasons detailed above, the rejections of the dependent claims are maintained.

C. Applicant argues on page 12 of the Supplemental Remarks that Lizardi only teaches RNA probes having the required structural features.

However, as noted in the new rejections above (as necessitated by the amendments) and in the response presented above, Lizardi et al clearly teach switch probes, of which Figures 12 and 13 are one example, have the added advantage of allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). In addition, Lizardi et al clearly teach switch probes that are DNA (column 6, lines 59-65). Further, Lizardi et al also clearly teach that probes of the invention of Lizardi et al contain "any desired sequence

(column 15, lines 15-22)," which is interpreted to mean any probe (i.e., the DNA probes described in column 6, lines 59-65) having the sequence configuration depicted in Figures 12-13.

Therefore, Lizardi et al suggest the probes of the invention (i.e., Figures 12-13) are DNA probes and thus do not require any ribozyme activity, as the probes allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20).

Thus, contrary to Applicant's arguments on pages 10-11 of the Supplemental Remarks, the teachings of Blackburn et al and Lizardi et al have been considered as a whole.

D. Applicant also argues on page 12 of the Supplemental Remarks that the only example of a DNA probe is that depicted in Figure 1, which does not meet the structural limitations of the instant claims and would move the redox label in the opposite direction than that of the instant claims.

However, as noted above, the broad teachings of Lizardi et al that switch probes in general (of which Figures 12 and 13 are but one example), have the added advantage of allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20). Thus, ribozyme-based detection is not specifically required of any probe.

In addition, Lizardi et al clearly teach switch probes that are DNA (column 6, lines 59-65).

Further, Lizardi et al clearly teach that probes of the invention of Lizardi et al contain "any desired sequence (column 15, lines 15-22)," which is interpreted to mean any probe (i.e., the DNA probes described in column 6, lines 59-65) having the sequence configuration depicted in Figures 12-13.

Therefore, Lizardi et al suggest the probes of the invention (i.e., Figures 12-13) are DNA probes and thus do not require any ribozyme activity, as the probes allowing selective generation of a detectable signal upon hybridization to the target (Abstract), wherein any number of different signal generating systems are linked to the detection of the switch (column 5, lines 15-20).

Thus, contrary to Applicant's reiterated arguments on pages 12-13 of the Supplemental Remarks, the teachings of Blackburn et al and Lizardi et al have been considered as a whole.

E. Applicant's remaining arguments on page 13 of the Supplemental Remarks rely on the alleged deficiencies of Blackburn et al in view of Lizardi et al. These alleged deficiencies are discussed above. Since the arguments regarding the alleged deficiencies of Blackburn et al in view of Lizardi et al were not persuasive for the reasons detailed above, the rejections of the dependent claims are maintained.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

11. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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